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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,689	07/13/2001	Boris Tartakovsky	TARTAKOVSKY 1	5905

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	09/806,689	TARTAKOVSKY ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-17 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-17 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 4/18/05 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment, remarks, and 1.132 declaration of Inventor Tartakovsky, filed 4/18/05, have been entered.

2. Claims 8-17 and 21 are pending and under examination.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 8-17 and 21 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the actions mailed 4/09/04 and 11/17/04.

Specifically, the specification provides insufficient evidence that the claimed method could be used to identify individuals with a high probability of having an HIV infection or monitor the efficacy of anti-HIV treatment.

As set forth previously, It is noted that given the language of the instant claims the claimed invention is intended to encompass significant breadth, i.e., methods of monitoring *any and all* types of infection, including but not limited to, bacterial, viral, fungal, and parasitic infections. For the invention to function then, it would be required that it be established that increased CD14 be present in the T cells of individuals suffering from *any and all* types of infections. Additionally, for the claimed method of monitoring the efficacy of a treatment to be enabled, it would be necessary that the specification establish that CD14 levels are reduced in response to efficacious treatment. Accordingly, it appears then that, given their novelty and considering their breadth, the enablement of the claimed methods would require a significant disclosure representative of all of the infections and all of the treatments encompassed by the claims. Said disclosure would most

obviously take the form of the measurement of CD14 in T cells in a representative number of infectious models or infection types, accompanied by the measure of the reduction of CD14 in T cells after a representative number of treatments of said infections. Additionally, other limitations (as discussed below) would also require enablement.

A review of the specification discloses just three relevant examples (4, 5, and 6), the data from which are set forth in Tables 1 and 2 and Figures 10, 11, and 12. Example 4 (Figures 10, 11, and 12) asserts that some individuals suffering from bacterial sepsis and HIV infection display increased MO2 in CD3+ cells. However, the figure legends disclose only "various kinds of infections" while Figures 10 and 12 themselves discloses only "infectious diseases" and Figure 11 itself discloses only "individuals". It is thus impossible to evaluate whether or not the diseases and subjects of the example are representative of those encompassed by the claims. In fact, the example and figures are essentially impossible to interpret given the lack of specific information disclosed in them. Example 5 (Table 1) discloses that MO2 is seen at higher levels in γ/δ T cells. It is unclear how this information could relate to the infected or treated individuals of the claims. Example 6 (Table 2) discloses that asymptomatic HIV+ patients show more MO2 in their T cells. Table 3 shows that 2 of 4 treated HIV+ patients showed a decrease in MO2 while 2 of 4 treated patients did not. In total then, it appears that the examples demonstrate only that: 1) MO2 may be increased in the T cells of HIV+ patients, and 2) that decrease in MO2 levels cannot be used as an accurate or reliable measure of the efficacy of treatment in HIV+ patients. This limited disclosure cannot be considered to be representative (nor enabling) of the scope of the claims.

Regarding additional limitations not enabled by the specification, there is no showing that the MO2 antigen is ever "expressed" by T cells. Indeed, the Inventors' own work (Tartakovsky et al., *Immunol. Letts.*, 2003) teaches that the protein is most likely not expressed at all by T cells, but rather it is internalized from an external source. Regarding the limitations of Claims 10-12 and 15-17 regarding the types of T cells employed in the comparisons to healthy cell populations, the specification discloses only that HIV+ CD8+ T cells show increased MO2 levels. In the case of CD4+ T cells, again only HIV+ cells are employed and in this instance the standard deviations approach (or exceed) the percentage of positive cells. Regarding γ/δ T cells, there is no disclosure comparing healthy to infected cells with any infectious agent.

Applicant's arguments, filed 4/18/05, have been fully considered but they are not persuasive. Applicant argues that the 1.132 declaration of Inventor Tartakovsky enables the method as now claimed. Accordingly, the declaration is addressed here.

The Inventor points to the first paragraph of page 10 of the specification,

"In accordance with an additional aspect of the invention, it has been shown that the level of MO2 cells may be a useful marker for monitoring the efficacy of a certain treatment administered to an in individual suffering from an infection. As mentioned above, infected individuals show a higher level of MO2 cells before receiving treatment as compared to the level of MO2 cells in healthy individuals. In accordance with the invention, it was shown that following treatment, the effect of the treatment may be monitored in the infected individuals on the

basis of the level of their MO2 cells following treatment. Routinely, the effect of treatment of a viral infection is monitored by measuring the viral load in the treated individual. In accordance with the invention, it has been shown that even when the viral load of treated infected individuals decreases in all the treated individuals, in some, the level of the MO2 cells remains significantly higher than the level of the cells in healthy individuals, while in other individuals following treatment the level of MO2 cells is reduced to the level of these cells in healthy individuals. Thus, the level of MO2 cells in treated infected individuals may be used as a basis for determining, on a cellar level, the effect of the treatment on the treated individual."

A careful review of the last sentence of this disclosure reveals that the specification actually discloses that *MO2 levels do not correlate with viral load.* This is a significant teaching given that viral load is routinely assayed as a measure of treatment efficacy. The Declarant appears to be arguing that the measure of MO2 is more important than the measure of viral load in the measurement of HIV treatment efficacy, an assertion that neither the prior art, nor the instant disclosure supports.

The Declarant presents a table showing that 3 of 5 patients showed increased lymphocyte, CD4+ cell, and CD8+ cell counts after HAART treatment. Note that the post-treatment cell counts are taken from 1-3 months post-treatment. The Declarant then argues that the cell counts of the table correlate with %CD8+MO2+ cells from (presumably) the same patients.

The Declarant's data is acknowledged, however, it is unclear how this data can support the method of the instant claims. First note that there is no finding, discussion, or argument that the method works for the detection of an individual with a high probability of having an HIV infection. Thus, the rejection of the method of Claims 8-12 has not been addressed. Regarding the method of monitoring the efficacy of anti-HIV treatment, the Declarant fails to disclose that the method of the instant specification was employed for the measurement of MO2 and, incredibly, fails to actually disclose the data regarding MO2+CD3+ and MO2+CD4+ cells. Most notably, a method of measuring the *percentage* of MO2+CD8+ cells is not the method of the instant claims - Claim 13 simply recites the measuring of the *number* of MO2+ cells in a sample.

And, as set forth previously, Applicant has again not addressed each of the arguments/grounds of rejection set forth by the Examiner above. For example, the specification discloses that only a small percentage of CD4+ T cells express MO2, while essentially all gamma/deltas T cells express MO2 (page 4) thus, it is unclear how these markers can be employed in the claimed method.

Regarding the method as now claimed, it is noted that the method has been significantly broadened by the instant amendment deleting most of the actual method steps from Claims 8, 9, 13, and 14. No longer is the method limited to the intracellular measurement of MO2 employing an antibody. No longer does the claimed method require fixing and permeabilizing the cells to be assayed. Indeed, the method is no longer limited to the use of an anti-MO2 antibody. It is the Examiner's position that the previously claimed method was not enabled and the much broader method of the instant claims is not either for additional reasons, e.g., there is no indication that the method can work in intact cells, and no disclosure of MO2-measuring methods, other than the intracellular assay if MO2 employing an anti-MO2 antibody.

Also note that the methods of the instant claims recite the measuring of only the *number* of MO2+ cells in a sample, not the *percentage* of MO2+ cells in a sample. There is no teaching in the specification, nor in Inventor Tartakovsky's 1.132 declaration, that simply counting MO2+ cells in a sample is an indication of anything. Finally note that claim 13 simply requires the counting of cells, and the finding of either *more* MO2+ cells or *fewer* MO2+ cells than in a sample obtained prior to treatment indicates efficacy of treatment. This claimed method makes no scientifically logical sense and is clearly not enabled.

Thus, for the reasons set forth above, it remains the Examiner's position that the limited disclosure of the specification is insufficient support for the methods of the instant claims.

5. The following are new grounds for rejection.

6. Claims 8-17 and 21 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) The deleting of steps ii - vii in Claims 8 and 13,

B) The deleting of the requirement for fixing and permeabilizing and the employment of Mabs which bind MO2 and T cell antigens in Claims 9 and 14.

Applicant's amendment, filed 4/18/05, fails to assert where support for the newly amended claims can be found. A review of the specification reveals no support for these much broader methods than were previously claimed, e.g., methods not requiring the use of an anti-MO2 antibody nor the use of fixed and permeabilized cells.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

9. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-

free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

7/7/05

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